reciting the term "about." The Action also states that claim 14 is indefinite for depending on non-elected claim 13 and for reciting a composition comprising an isolated polynucleotide inconsistent with a composition comprising an isolated polypeptide recited in claim 13.

Applicants respectfully traverse this ground of rejection related to the term "about." Applicants submit that the term "about" in claims 1-3 does not render these claims indefinite. The Federal Circuit held that the term "about" (as used in expression such as "about 100% per second") as well as other terms (*e.g.*, "close to," "closely approximate" and "close proximity") are not too vague to satisfy the requirements of indefiniteness under 35 U.S.C. § 112. *Andrew Corp. v. Gabriel Electronics*, 847 F.2d 819, 6 USPQ2d 2010, 2012-13 (Fed. Cir. 1988). The court stated that "such words are ubiquitous in patent claims, and that such usages, when serving reasonably to distinguish the claimed subject matter from the prior art, have been accepted in patent examination and upheld by the courts." *Id.* In *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 UAPQ 81, 95 (Fed. Cir. 1986), the court found that a claim to a process for determining the presence of an antigenic substance in a fluid was not indefinite for reciting the use of first and second monoclonal antibodies that have an affinity for the antigenic substance of at least about 108 liters per mole. The court stated that although the calculated affinity was not precise, the claim, read in light of the specification, reasonably apprises those skilled in the art and is as precise as the subject matter permits, and that "[a]s a matter of law, no court can demand more." *Id.* at 95. Applicants respectfully submit that the instant case is similar to *Andrew Corp.* and *Hybritech* in that the term "about" serves reasonably to define the claimed invention, thus does not render the claims reciting this term indefinite.

Applicants wish to thank the Examiner for noting the inadvertent informalities in claim 14. As set forth above, Applicants have redrafted claim 14 in an independent form to eliminate such informalities and, therefore, this rejection has been obviated.

In view of the above remarks, Applicants submit that the grounds of rejection under 35 U.S.C. § 112, second paragraph, have been overcome. Accordingly, withdrawal of these rejections is respectfully requested.

Rejections under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 1-9 and 14 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly being non-enabled. More specifically, the Action asserts that the specification does not reasonably provide enablement for (1) an isolated nucleic acid molecule comprising a polynucleotide at least 90% identical to SEQ ID NO:3; (2) an isolated nucleic acid comprising a polynucleotide encoding a polypeptide having a sequence identical to SEQ ID NO:4 or a portion of SEQ ID NO:4 except for at least one conservative amino acid substitution; (3) the use of SEQ ID NO:3 for gene therapy; (4) a polynucleotide encoding amino acids from about 1 to about 115 of SEQ ID NO:4 as recited in claims 1c and 3, or from about 2 to about 115 of SEQ ID NO:4 as recited in claims 1d and 3; (5) the complement of the polynucleotide of 1c or 1d; (6) any isolated nucleic acid molecule comprising the about 345 contiguous nucleotides from the coding region of SEQ ID NO:3 as recited in claim 2; (7) any of these isolated nucleic acid molecules that are anything other than DNA; and (8) any composition comprising an isolated polynucleotide encoding amino acids from about 4 to about 50 or from about 9 to about 45 of SEQ ID NO:4 as recited in claim 13.

Applicants respectfully traverse these grounds of rejection. Claim 1 has been amended and now recites, in pertinent part, an isolated nucleic acid molecule comprising a polynucleotide at least 90% identical to a polynucleotide encoding a polypeptide comprising amino acids from about 1 to about 115 of SEQ ID NO:4 or amino acids from about 2 to about 115 of SEQ ID NO:4, wherein said polynucleotide encodes a polypeptide that has mitogenic activity. Applicants submit that one of skill in the art is able to make and use a polynucleotide wherein the amino acid sequence encoded by that polynucleotide is specified and the activity of the polypeptide produced therefrom may be assessed with at most routine experimentation.

Claim 3 has been amended to recite that the polypeptide has at least one conservative amino acid substitution, at least 90% identity with SEQ ID NO:4, and mitogenic activity. Applicants submit that it is within the ordinary skill in the art to design and make a polynucleotide that encodes a full-length or partial polypeptide set forth in SEQ ID NO:4 with at least one conservative amino acid substitution, as described in the specification (*see, e.g.*, page 11, lines 16-17; and page 15, line 28 through page 16, line 7). The specification also provides algorithms useful for determining percent identity or percent conservation between variant

sequences (*see, e.g.*, specification at page 8, lines 18-22, and at page 10, line 25 through page 11, line 17). Additionally, the specification provides guidance to a person having ordinary skill in the art to test or verify, by at most routine experimentation, the mitogenic activity of polypeptides having at least 90% identity with SEQ ID NO:4 (*see, e.g.*, specification at pages 38-39, Example 3).

Regarding the concerns in the Action related to the use of SEQ ID NO:3 for gene therapy, without acquiescing to the assertions in the Action, Applicants submit that it is not determinative to the enablement analysis whether SEQ ID NO:3 is enabled for gene therapy. Applicants respectfully submit that the alleged lack of enablement for gene therapy is beside the point as this polynucleotide has utilities other than gene therapy, such as making recombinant EGFH2 protein. Furthermore, the claim that recites SEQ ID NO:3 (*i.e.*, claim 2) is not directed to a method of using SEQ ID NO:3 for gene therapy, but directed to a composition of matter, an isolated nucleic acid molecule. Applicants submit that the enablement requirement for claim 3 has been satisfied because the present application provides enabling descriptions for making and using SEQ ID NO:3, such as making a recombinant EGFH2 protein.

Regarding the remaining concerns in the Action, which are related to polynucleotides encoding partial or full length sequences of SEQ ID NO:4 and complements thereof, Applicants submit that it is within the ordinary skill in the art to make and use such polynucleotides, given the disclosure of SEQ ID NO:4 provided by the present application. It is noted that the view point for enablement determination is that of one of ordinary skill in the art. Thus, the knowledge possessed by one of the ordinary skill in the art needs not be explicitly described in an application. Applicants are unclear about the concerns related to reading frames of the claimed polynucleotides: It appears that in the Action, the term "about" is interpreted as including a portion of a codon. Applicants submit that the term "about" as recited in the pending claims, such as "amino acids from about 1 to about 115 of SEQ ID NO:4," refers to, for example, amino acids from 1 to 115, from 2 to 115, from 1 to 114, from 2 to 114 of SEQ ID NO:4, and the like; it does not indicate that the claimed polynucleotide has a partial codon for amino acid 1 or amino acid 115 of SEQ ID NO:4.

In view of the above remarks, Applicants submit that the grounds of rejection under 35 U.S.C. § 112, first paragraph, has been overcome. Withdrawal of these rejections is respectfully requested.

Rejections under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 1-9 and 14 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking an adequate written description. More specifically, it is asserted in the Action that the specification does not provide sufficient support for any polynucleotide sequence that is 90% identical to SEQ ID NO:3, a nucleic acid molecule comprising about 345 contiguous nucleotides from the coding region of SEQ ID NO:3, any polynucleotide other than SEQ ID NO:3 encoding any amino acid sequence other than SEQ ID NO:4, any complement of a polynucleotide other than to SEQ ID NO:3, any nucleotide sequence that has been mutated so that at least one conservative amino acid substitution has been made that encodes SEQ ID NO:4, any other polynucleotide to be used in a vector to be placed in a host cell to produce any polypeptide other than SEQ ID NO:4, or any polynucleotide to be used in *in vivo* gene therapy.

Applicants respectfully traverse these grounds of rejection and submit that the claims are directed to subject matter clearly described in the instant specification, which would convey to a person having ordinary skill in the art that Applicants had possession of the claimed invention at the time of filing. As disclosed in the specification and recited in the claims, the instant invention is directed, in pertinent part, to an isolated nucleic acid molecule comprising a polynucleotide at least 90% identical to a polynucleotide encoding a polypeptide comprising from about 1 to about 115 or from about 2 to about 115 of SEQ ID NO:4, wherein said polynucleotide encodes a polypeptide that has mitogenic activity. As noted in the Office Action, a "description of a genus of polynucleotide sequences may be achieved by means of a recitation...of structural features common to the genus" (Office Action at page 8, middle paragraph citing *Regents of University of California v. Eli Lilly & Co.*, 43 U.S.P.Q.2d 1398, 1406, Fed. Cir. 1998). Applicants respectfully submit that the instant specification describes an actual reduction to practice of a human EGFH2 polynucleotide encoding amino acids from about 1 to about 115 or from about 2 to about 115 of SEQ ID NO:4 (*see, e.g.*, specification at page 36, Example 1, and Figure 2). That is, a nucleic acid molecule comprising about 345 contiguous

nucleotides from the coding region of SEQ ID NO:3 was reduced to practice. Consequently, the human EGFH2 polynucleotide sequence as described in the instant specification is representative of the genus of claimed polynucleotide sequences because each polynucleotide sequence has at least 90% structural identity with a polynucleotide encoding amino acids from about 1 to about 115 or from about 2 to about 115 of SEQ ID NO:4.

Moreover, Applicants respectfully submit that the instant specification describes methods for identifying a polypeptide or variant thereof that has mitogenic activity (*see, e.g.*, specification at page 10, lines 13-20, and Example 3). Hence, the various polynucleotides at least 90% identical to a polynucleotide encoding a polypeptide comprising from about 1 to about 115 or from about 2 to about 115 of SEQ ID NO:4 and having mitogenic activity could be easily identified by a person having ordinary skill in the art with at most routine experimentation. Consequently, each of the claimed polynucleotides (*i.e.*, the genus of polynucleotides) have both a structural identity and a specified biological activity, as provided by the invention. In addition, as described in the specification (*see, e.g.*, page 14, line 17-24; page 15, lines 8-15) and as was known in the art at the time of filing, methods were available to make variant and derivative polynucleotides which have 90% identity to a polynucleotide encoding amino acids from about 1 to about 115 or from about 2 to about 115 of SEQ ID NO:4. The specification also provides algorithms useful for determining percent identity or percent conservation between variant sequences (*see, e.g.*, specification at page 8, lines 18-22, and at page 10, line 25 through page 11, line 17). Therefore, a person having ordinary skill in the art would conclude that Applicants were in possession of the necessary attributes possessed by polynucleotides at least 90% identical to a polynucleotide encoding a polypeptide comprising from about 1 to about 115 or from about 2 to about 115 of SEQ ID NO:4, wherein the encoded polypeptide has mitogenic activity (*see also* "Revised Interim Written Description Guidelines Training Materials," at page 53, Example 14, www.uspto.gov).

As noted above, an adequate written description of the invention may be shown by *any* description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention (*see* Guidelines for Examination of Patent Applications under the 35 U.S.C § 112, First Paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, at 1105). Applicants further submit that there is a

strong presumption that an adequate written description of the claimed invention is present in the specification as filed. *Id.* Accordingly, Applicants respectfully submit that the instant specification adequately describes the subject matter encompassed by the claims so as to reasonably convey to a person having ordinary skill in the art that Applicant, at the time of filing the instant application, had possession of the claimed invention. Thus, Applicant requests that this rejection be withdrawn because the requirements under 35 U.S.C. §112, first paragraph have been satisfied.

Objections to Drawings

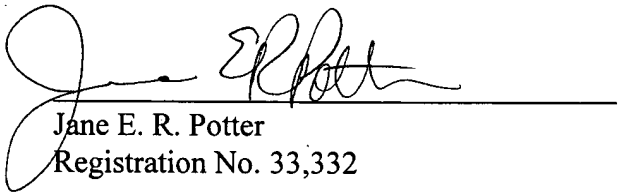
The drawings stand objected to for technical errors. Formal drawings are being filed herewith.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings to Show Changes Made.**"

All of the pending claims in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Seed Intellectual Property Law Group PLLC



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(JEP:cew) #266823

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The following paragraph has been added at line 4 of page 1:

CROSS-REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. Provisional Patent Application No. 60/149,986 filed August 20, 1999, where this provisional application is incorporated herein by reference in its entirety.

In the Claims:

Claims 1-3, and 14 have been amended as follows:

1. (Amended) An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:

~~(a) a polynucleotide encoding amino acids from about 1 to about 115 of SEQ ID NO:2;~~

~~(b) a polynucleotide encoding amino acids from about 2 to about 115 of SEQ ID NO:2;~~

~~(c)~~(a) a polynucleotide encoding ~~amino acids~~ a polypeptide comprising from about 1 to about 115 of SEQ ID NO:4;

~~(d)~~(b) a polynucleotide encoding ~~amino acids~~ a polypeptide comprising from about 2 to about 115 of SEQ ID NO:4;

~~(e)~~(c) ~~the~~ a polynucleotide complement of the polynucleotide of (a)~~,~~ or (b)~~, (c), or (d)~~; and

~~(f)~~(d) a polynucleotide at least 90% identical to the polynucleotide of (a)~~,~~ or (b)~~, (c), (d) or (e)~~ wherein said polynucleotide encodes a polypeptide that has mitogenic activity.

2. (Amended) An isolated nucleic acid molecule comprising about 345 contiguous nucleotides from the coding region of ~~SEQ ID NO:1 or~~ SEQ ID NO:3.

3. (Amended) An isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide having an amino acid sequence from about 1 to about 115 or from about 2 to about 115 of SEQ ID NO:4, wherein said polypeptide ~~, except for~~ has at least one conservative amino acid substitution~~,~~ at least 90% identity with SEQ ID NO:4, and mitogenic activity~~said polypeptide has an amino acid sequence selected from the group consisting of:~~

~~(a) amino acids from about 1 to about 115 of SEQ ID NO:2;~~

~~(b) amino acids from about 2 to about 115 of SEQ ID NO:2;~~

~~(c) amino acids from about 1 to about 115 of SEQ ID NO:4; and~~

~~(d) amino acids from about 2 to about 115 of SEQ ID NO:4~~.

4. The isolated nucleic acid molecule of claim 1, which is DNA.

5. A method of making a recombinant vector comprising inserting a nucleic acid molecule of claim 1 into a vector in operable linkage to a promoter.

6. A recombinant vector produced by the method of claim 5.

7. A method of making a recombinant host cell comprising introducing the recombinant vector of claim 6 into a host cell.

8. A recombinant host cell produced by the method of claim 7.

9. A recombinant method of producing a polypeptide, comprising culturing the recombinant host cell of claim 8 under conditions such that said polypeptide is expressed and recovering said polypeptide.

14. (Amended) A composition comprising an isolated polynucleotide encoding a polypeptide~~ of claim 13~~ comprising an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence from about 4 to about 50 of SEQ ID NO:4;

(b) an amino acid sequence from about 9 to about 45 of SEQ ID NO:4; and

(c) an amino acid sequence at least 86% identical to said amino acid sequence of (a) or (b), wherein said polypeptide has mitogenic activity.

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